ABSTRACT OF THE DISCLOSURE

The present invention provides methods for identifying improved folate
antagonists. The improved folate antagonists identified by the methods of the
invention have increased selectivity. The increased selectivity of the folate
antagonists results in a reduced risk of adverse effects following treatment with the
improved folate antagonists. The improved folate antagonists are identified based on
their reduced binding affinity for at least one enzyme selected from glutathione
synthase, pyruvate carboxylase, propionyl-CoA carboxylase, biotin carboxylase,
acetyl-CoA carboxylase, and methylcrotonyl-CoA carboxylase. According to the
invention, folate antagonists having reduced affinity for at least one enzyme selected
from this group of enzymes are selected for the treatment of neoplastic,
hyperproliferative, and immune disorders.

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